

Application No.: 10/623035

Docket No.: BPI-193  
(PATENT)

In the claims:

Please amend claims 17 and 18 as follows.

1. **(Original)** A method of treating pain in a subject comprising administering to the subject a therapeutically effective amount of a neutralizing, high affinity TNF $\alpha$  antibody, such that said pain is treated.
2. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3}$  s $^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an IC $_{50}$  of  $1 \times 10^{-7}$  M or less.
3. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof with the following characteristics:
  - a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3}$  s $^{-1}$  or less, as determined by surface plasmon resonance;
  - b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
  - c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.
4. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

Application No.: 10/623035

Docket No.: BPI-193  
(PATENT)

5. (Original) The method of any one of claims 1, 2, 3, or 4, wherein the antibody is D2E7.
6. (Original) The method of any one of claims 1, 2, 3, or 4, wherein the pain is neuropathic pain.
7. (Original) A method for treating a subject suffering from pain, comprising administering to the subject an antibody, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less, such that the pain is treated.
8. (Original) A method for treating a subject suffering from pain, comprising administering to the subject an antibody such that the pain is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof with the following characteristics:
- a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;
  - b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
  - c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that the pain is treated.
9. (Original) A method for treating a subject suffering from pain in which TNF $\alpha$  activity is detrimental, comprising administering to the subject an antibody such that the pain is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion

Application No.: 10/623035

Docket No.: BPI-193  
(PATENT)

thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that the pain is treated.

10. (Original) The method of any one of claims 7, 8, or 9, wherein the antibody is D2E7.
11. (Original) The method of any one of claims 7, 8, or 9, wherein the pain is neuropathic pain.
12. (Original) A method for treating a subject suffering from pain in which TNF $\alpha$  activity is detrimental, comprising administering to the subject D2E7 such that the pain is treated.
13. (Original) The method of claim 12, wherein the pain is neuropathic pain.
14. (Original) A method of treating neuropathic pain comprising administering to a subject suffering from neuropathic pain a therapeutically effective amount of an antibody, or an antigen-binding portion thereof, that dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less, such that the neuropathic pain is treated.
15. (Original) The method of claim 14, wherein the antibody is D2E7.
16. (Original) A method for treating neuropathic pain comprising administering to a subject suffering from neuropathic pain an effective amount of D2E7.
17. (Currently amended) A kit comprising:
  - a) a pharmaceutical composition comprising a human TNF $\alpha$  antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody

Application No.: 10/623035

Docket No.: BPI-193  
(PATENT)

dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3}$  s $^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less; and

b) instructions for administering to a subject the TNF $\alpha$  antibody pharmaceutical composition for treating a subject who is suffering from pain.

18. (Currently amended) A kit according to claim 17, wherein the TNF $\alpha$  antibody, or an antigen binding portion thereof, is D2E7